TB Notes
Spring 1994

Dear Colleague:

This spring, staff in the Division of Tuberculosis Elimination (DTBE) attended several meetings on tuberculosis (TB) control. In May many of us went to the 1994 International Conference of the American Thoracic Society/American Lung Association in Boston, where there were several sessions on TB. At this meeting I announced the 1993 TB morbidity data, published in the May 27 issue of the *Morbidity and Mortality Weekly Report.* Because of close collaboration between DTBE and reporting areas throughout the United States, I was able to release the data relatively early in the year.

Also, on April 15 Dr. Nancy Binkin and I attended a meeting in El Paso, Texas, on binational TB control issues. At this meeting, representatives from California, Arizona, New Mexico, Texas, Mexico, and the Pan American Health Organization (PAHO) discussed strategies for controlling TB in the U.S.-Mexico border area.

We are planning two major meetings for this summer. The first, scheduled for August 1-3 in Atlanta, is a workshop for selected participants on the diagnosis, treatment, and control of TB in children in the United States. The second meeting, scheduled for August 28-30 in Bethesda, Maryland, will focus on behavioral issues in TB treatment and control. This meeting is sponsored by CDC, the National Institute on Drug Abuse, the National Heart, Lung, and Blood Institute, and the National Institute for Nursing Research. The goals are to determine key behavioral research questions related to TB, stimulate research on the behavioral aspects of TB prevention and control, coordinate the TB behavioral research activities of participating researchers, and publish a monograph describing research priorities.

In May CDC and the American Thoracic Society issued new guidelines for the treatment of TB disease and infection. For a summary of the major changes in these guidelines, see the related article in this issue of *TB Notes*.

Starting in June, health care workers and others throughout the country will have access to information on TB through CDC's fax information service. Since 1987, this service has provided callers with fax sheets on various topics, such as childhood immunizations, hospital infection control, human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), and other diseases; recently TB was added to the list of topics. Callers may receive fax sheets on TB treatment, diagnosis, BCG, infection control, screening, and morbidity; general information on TB is available for the public. To use the service, call (404) 332-4565 and follow the prompts.

Kenneth G. Castro, M.D.

In This Issue

NOTE: The use of trade names in this issue is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

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HIGHLIGHTS FROM STATE AND LOCAL PROGRAMS

Trust, a Key Ingredient in Community Outreach

In Iowa, disease prevention specialists from the state health department are occasionally asked to assist public health nurses in follow-up activities. Rebecca Rameriz-Corona, one of the disease prevention specialists in Polk County, has been instrumental in working with the local Hispanic/Latino community.

Ms. Rameriz came to the Iowa Department of Public Health in June 1989. She had recently graduated from the University of Iowa with a bachelor's degree in Spanish. Although she did not have public health experience, she had worked with the League of United Latin American Citizens (LULAC) as a volunteer while she was in college. This work with LULAC helped Ms. Rameriz develop networking skills within the Hispanic/Latino community, as well as the ability to identify resources for those in need.

Since she moved to Polk County, Ms. Rameriz has established herself as a part of the Hispanic/Latino community, worshipping, shopping, and socializing within the community. In addition, Ms. Rameriz's work as a disease prevention specialist and her personal commitment to being a resource has established

her as a trusted community leader. "I have done a lot of things for them [the Hispanic/Latino community] that go beyond my job," she said.

Ms. Rameriz's involvement in the community has paid off. For example, she was a great asset in a follow-up investigation for a case of drug-resistant TB in a local meat packing plant where many employees are Hispanic/Latino. She was able to persuade the workers to get skin tested, and she worked with the managers of the plant to ensure that the follow-up investigation went smoothly. The main key to her success: both the employees and the managers saw her as a member of their community, not just a representative of the government.

Ms. Rameriz uses many avenues to reach the Hispanic/Latino community. For example, she goes to ethnic stores, a community center, and two popular churches to distribute flyers and pass the word for activities such as immunization and TB screening clinics for the community. These places are also crucial for reaching persons who are not yet established in the community.

Ms. Rameriz has not forgotten the value of knowing resources in the community for other needs. With this in mind, she has nurtured a relationship with several local and state agencies. Often the link between these programs and the community, Ms. Rameriz makes referrals and explains program policies. However, her credibility with community members is undermined when program policies change after she has explained them to community members. In these situations, Ms. Rameriz has found it very helpful to explain in detail why the change occurred. On the whole, being open and straightforward has helped Ms. Rameriz maintain the trust of the persons she seeks to help.

—Reported by Ralph Wilmoth
Iowa TB program

Mobile Homes: The Rural Equivalent of SRO Hotels

Rural areas seldom provide access to single-room occupancy (SRO) facilities; so when the need arises to provide shelter for a TB patient, the Mississippi TB program improvises.

Mobile homes offer one inexpensive alternative that is commonly available, even in remote areas. The mobile home might be a single rental property or one of a group in a mobile home or trailer park. Mobile homes have several advantages: they are usually self-contained, they do not share ventilation with other units, and they are generally available on a weekly or monthly rental basis. Like the SRO facility, the mobile home provides the opportunity to isolate and anchor the patient to a particular location for the administration of directly observed therapy.

Cottage-type motel units offer the same advantages as mobile homes — for example, the units do not share ventilation — but they are less

commonly available. Like SRO facilities, the cottage-type motel is, as a rule, no longer a state-of-the-art facility. Managers of these units appreciate the business and are often willing to negotiate rent for extended occupancy.

When negotiating housing or shelter for a patient, the TB program should establish the agreement, rules, and expectations up front and make sure that the patient fully understands and abides by the agreement. This is important, because the ability of the TB program to control the patient will be considered in future negotiations. In Mississippi, the agreements are negotiated locally by the district TB nurse or the county public health nurse in consultation with the TB program.

—Reported by Mike Holcombe
Mississippi TB program

New York City Uses AT&T Language Line Service

The AT&T Language Line Service, an over-the-telephone translation service, is being used in New York City chest clinics. The language line offers a pool of approximately 140 languages, 24 hours a day, 7 days a week. Based in Monterey, California, it covers all of the United States and Canada. All operators are familiar with medical terms.

Clinic staff have used the service to provide information about TB to non–English-speaking patients when no on-site translator is available. Fort Greene Clinic, for example, has used the service to advise a Czech-speaking

patient who was traveling home about how to continue treatment.

Cost-effectiveness is an important consideration for the chest clinic. Lengthy patient interviews to explain treatment and identify contacts could take hours on the language line. The cost for the service ranges from $2.20 a minute to $4.50 a minute, depending on the language chosen and the time of day.

The consensus among the clinics is that the language line should not replace efforts to recruit and train multilingual staff to provide TB-related services. Nevertheless, the clinics serve many high-risk immigrants who do not speak English, and the language line has helped remove a barrier that these patients face in receiving health care. All indications are that the clinics have been satisfied with the service.

—Reported by Mitchell Holtzman
New York City TB program

Photos of Patients: An Aid in Directly Observed Therapy

In San Francisco, staff of the TB program have found it useful to have a photograph of patients who are receiving directly observed therapy (DOT). This way, staff who are making field visits can easily identify the patients who are receiving medication. The photos are particularly helpful for staff who are seeking patients on the streets or in other public places for DOT.

When a patient begins DOT, the staff explain to him or her why it would be helpful to have a photo. If the patient agrees to be photographed, he or she signs a consent form before the color Polaroid photo is taken. When assured that the photo will be used only by clinic staff — never for police or immigration purposes — most patients readily agree to have their picture taken.

The photographs have proved useful in other ways. When attached to the front of DOT charts, the photos allow staff to locate these charts quickly and return them to a special DOT chart filing system. In many cases, the photos document marked improvement in patients as they progress through their treatment. Staff, or often patients themselves, will suggest replacing the initial photo with a photo taken later in the course of treatment. This gives staff and patients an opportunity to acknowledge the positive effects of treatment in patients who have adhered to therapy.

—Reported by Houmpheng Banouvong
San Francisco TB program

CDC and ATS Issue New Treatment Guidelines for TB

In May CDC and the American Thoracic Society (ATS) published new guidelines for the treatment of TB disease and infection.[1] The new treatment statement, published in the *American Journal of Respiratory and Critical Care Medicine,* replaces the statement issued in 1986.[2] The major changes and additions are summarized below; a comparison with the 1986 statement follows in italics. [Note: this is a summary of *changes* in the new guidelines, not a summary of the guidelines themselves.]

Treatment of TB

1. Four-Drug Regimen for Initial Therapy
   A four-drug regimen is recommended for the initial therapy of TB, except when there is little possibility of drug resistance (i.e., there is less than 4% primary resistance to isoniazid in the community, and the patient has had no previous treatment with antituberculosis medications, is not from a country with a high prevalence of drug resistance, and has no known exposure to drug-resistant TB).

Previously, a three-drug regimen was recommended for initial therapy, and the addition of ethambutol was recommended only if isoniazid resistance was suspected. Also, the previous statement recommended daily therapy for the first 2 months followed by daily or twice-weekly therapy. The new statement gives two more options: (1) twice-weekly therapy after an initial 2-week period of daily therapy or (2) fully intermittent therapy (three-times-weekly therapy from the beginning) when four drugs are given for the entire 6 months of treatment.

2. Six-Month Regimen for HIV-Infected Persons
   The recommendations for the duration of treatment for TB in HIV-infected persons are the same as for persons not infected with HIV. However, in HIV-infected patients it is critically important to assess the clinical and bacteriologic response

to therapy. If there is evidence of slow or suboptimal response, therapy should be prolonged as judged on a case-by-case basis.

Treatment for HIV-infected persons was not discussed in the 1986 statement, but in other statements since 1986, CDC has recommended longer therapy for HIV-infected persons. Recent data indicate that most HIV-infected persons respond well to short-course therapy. However, longer therapy is recommended for TB infection in HIV-infected persons (see p.9).

3. More Widespread Use of Directly Observed Therapy
   Consideration should be given to treating all patients with directly observed therapy.

Directly observed therapy was specifically recommended only for persons whose treatment had failed or who had relapsed, although ensuring adherence was emphasized for all patients.

4. Minimum of 12 Months of Therapy for Children with Some Forms of Extrapulmonary TB
   In general, extrapulmonary TB should be managed according to the principles and with the drug regimens outlined for pulmonary TB. In children, however, a minimum of 12 months of therapy is recommended for miliary TB, bone and joint TB, or tuberculous meningitis.

Previously, it was stated that longer therapy may be necessary for lymphadenitis and bone and joint TB. A 12-month regimen for children was not specified.

5. A 4-Month Regimen for Smear- and Culture-Negative TB
   A 4-month regimen of isoniazid and rifampin, preferably with pyrazinamide for the first 2 months, is acceptable therapy for adults who have active TB and who are sputum smear and culture negative, if there is little possibility of drug resistance.

No specific regimen for smear- and culture-negative TB was recommended in the 1986 statement.

6. Fixed Drug Combinations to Enhance Adherence
   The use of fixed drug combinations is strongly encouraged in adults to enhance patient adherence and reduce the risk of inappropriate monotherapy.

This was not mentioned in the previous statement.

7. Regimens for Isoniazid-Resistant TB
   For TB resistant only to isoniazid, a 6-month regimen of isoniazid, rifampin, pyrazinamide, and either ethambutol or streptomycin is effective. When isolated isoniazid resistance is documented, isoniazid should be discontinued and pyrazinamide should be continued for the entire 6 months of therapy. When isoniazid resistance is documented in the 9-month regimen without pyrazinamide, isoniazid should be discontinued. If ethambutol was included in the initial regimen, treatment with rifampin and ethambutol should be continued for a minimum of 12 months. If ethambutol was not included initially, susceptibility tests should be repeated, isoniazid should be discontinued, and two new drugs (e.g., ethambutol and pyrazinamide) should be added.

Only the regimen of rifampin and ethambutol for 12 months was discussed in the previous statement.

8. Multidrug-Resistant TB
   Multidrug-resistant TB (i.e., TB resistant to at least isoniazid and rifampin) presents difficult treatment problems. Treatment must be individualized and based on susceptibility studies. In such cases, consultation with a medical expert is recommended. Because of the poor outcome in such cases, it is preferable to give at least three new drugs to which the organism is susceptible. The regimen should be continued at least until bacteriologic sputum conversion is documented, followed by at least 12 months of two-drug therapy. Often a total of 24 months of therapy is given empirically. The role of new agents, such as the quinolones and amikacin, in the treatment of multidrug-resistant disease is not known, although these drugs are commonly being used in such cases. Finally, surgery appears to offer considerable benefit and significantly improve cure rates for patients in whom the bulk of disease can be resected.

Multidrug-resistant TB was not addressed in the 1986 statement. Of note, many clinicians recommend at least 18 to 24 months of multidrug therapy after culture conversion.

Treatment of TB Infection

1. Treatment of TB Infection in Children
   For infants and children younger than 4 years old who have no other risk factors, a reaction of $\geq$10 mm is considered positive. The American Academy of Pediatrics recommends

that children receive 9 months of therapy for TB infection.

The different cutpoints were not specifically discussed in the previous statement. Also, this is the first time that children younger than 4 years old who have no other risk factors have been mentioned specifically; they were not included in the 10-mm cutpoint group in the 1990 Diagnostic Standards and Classification of TB.

2. Treatment of TB Infection in HIV-Infected Persons
   For adults and children with HIV infection, a reaction of ≥5 mm is considered positive. Persons with a positive skin test result and HIV infection should be considered for preventive therapy regardless of their age. Anergic HIV-infected adults at increased risk for TB should also be considered for preventive therapy. Twelve months of preventive therapy is recommended for adults and children with HIV infection and other conditions associated with immunosuppression.

In the previous statement, preventive therapy was recommended for HIV-infected persons; however, the duration of preventive therapy, as well as a specific cutpoint for the tuberculin skin test results, was not discussed.

3. Regimens for Persons with an Abnormal Chest Radiograph or Silicosis
   In patients who have a positive tuberculin skin test result and either silicosis or a chest radiograph demonstrating old fibrotic lesions, and who have no evidence of active TB, acceptable regimens include (1) 4 months of isoniazid plus rifampin, or (2) 12 months of isoniazid if infection with drug-resistant organisms is judged to be unlikely.

The 4-month regimen is a new recommendation based on recent studies.

4. Directly Observed Preventive Therapy
   As with treatment for TB, the success of preventive therapy depends on whether patients adhere to the prescribed regimen. Although not evaluated in clinical studies, directly observed preventive therapy may be

used for at-risk adults and children who cannot or will not reliably self-administer therapy.

Directly observed preventive therapy was not mentioned in the 1986 statement.

5. Treatment of TB Infection in Pregnant Women
   Although no harmful effects of isoniazid to the fetus have been observed, preventive therapy is generally delayed until after delivery. There does not appear to be any substantial increase in TB risk for women as a result of pregnancy. However, for pregnant women who are likely to have been recently infected or who have high-risk medical conditions, especially HIV infection, isoniazid preventive therapy should begin when the infection is documented.

In the previous statement, preventive therapy was recommended for newly infected pregnant women after the first trimester; preventive therapy for HIV-infected pregnant women was not discussed.

6. Monitoring During Preventive Therapy
   All persons receiving preventive therapy should be questioned at monthly intervals about symptoms of adverse reactions. In addition, in persons 35 years and older, hepatic enzymes should be measured before the start of isoniazid preventive therapy and monitored monthly throughout treatment. The factors associated with an increased risk for hepatitis include age greater than 35, the daily use of alcohol, chronic liver disease, and injection drug use. Also, some evidence suggests that black and Hispanic women are at greater risk for fatal hepatitis. Persons taking certain medications concurrently with isoniazid may be at increased risk for hepatitis or drug interactions. More careful monitoring should be considered for these groups; this may include more frequent laboratory monitoring.

In the previous statement, laboratory monitoring was recommended only for persons 35 years of age and older.

—Reported by Pattie Simone, MD
Division of TB Elimination

References

1. American Thoracic Society. Treatment of tuberculosis and tuberculosis infection in adults and children. *Am J Respir Crit Care Med.* 1994;149:1359-1374.

2. American Thoracic Society. Treatment of tuberculosis and tuberculosis infection in adults and children. *Am Rev Respir Dis.* 1986;134:355-363.

Tuberculosis Database System Version 5.6 Released

In April, DTBE released the 5.6 version of the TB Database System (TBDS). The upgraded software was distributed via WONDER e-mail during the week of April 25 to most state and big-city TB control officers and field staff. From now on, DTBE will support only the 5.6 version; TBDS will not be updated again before the Tuberculosis Information Management System (TIMS) is released.

The new software can be installed on a local-area network (LAN) or on a single-user system. When installed on a LAN, the software can be used by several persons at the same time. Some other improvements: improved searches, revised summary reports, revised planning reports, and the automatic generation of tracer files. Tracer files list the persons included in each program management report, as well as the categories for each of these persons.

The manual for TBDS has not been upgraded, but support for the new system is just a phone call away. If you encounter a problem with TBDS, call Rich Niersbach at (404) 639-8125 or Craig Studer at (404) 639-8135 during regular business hours.

—Reported by Craig Studer
Division of TB Elimination

Issues in Surveillance for HIV/AIDS and TB

On January 1, 1993, the surveillance case definition for acquired immunodeficiency syndrome (AIDS) among adolescents and adults was expanded beyond the surveillance definition published in 1987[1] to include all HIV-infected persons with severe immunosuppression (<200 CD4+ T-lymphocytes/µL or a CD4+ T-lymphocyte percentage of total lymphocytes of <14), recurrent pneumonia, invasive cervical cancer, or pulmonary TB. During 1993, 103,500 AIDS cases were reported in the United States in persons 13 years of age and older, an increase of 111% over the 49,016 reported in 1992.[2] Approximately 54% (55,432) of the cases were reported based on conditions added to the definition in 1993; for 3,988 (7%) of these, the only condition was pulmonary TB diagnosed since 1978. All states have specific TB and AIDS reporting laws that require reporting to local and/or state health departments. In many health departments, TB and AIDS programs are administratively and physically separate. The revision of the AIDS surveillance case definition increases the need for better communication between these two surveillance systems to ensure the accuracy of information and the best provision of services to HIV-infected persons with TB infection or disease.

In addition to extrapulmonary TB, pulmonary TB should be reported to AIDS surveillance programs according to criteria in the 1990 TB case definition

for public health surveillance.[3] This case definition has three components:

1. Laboratory-confirmed cases diagnosed by isolation of *M. tuberculosis* from a clinical specimen.

2. Cases for which acid-fast bacilli (AFB) have been found in a clinical specimen, but for which a culture has not been or cannot be obtained (e.g., disease in a person diagnosed with TB at death based on positive sputum for AFB or histologic evidence on a pathology specimen).

3. Cases that meet all four of the following clinical criteria: (1) a positive tuberculin skin test result, (2) other signs and symptoms compatible with TB, such as an abnormal, unstable (worsening or improving) chest radiograph, or clinical evidence of current disease, (3) treatment with two or more antituberculosis medications, and (4) a completed diagnostic evaluation.

Cases that meet all the criteria in any one of the three components are classified as verified TB cases according to the TB surveillance case definition. Cases that do not meet all the criteria in any one of the three components (e.g., disease in anergic patients who have a negative culture for *M. tuberculosis* but who have a clinical syndrome consistent with TB) may be reported to the TB programs by the health care provider and verified as TB cases based on provider diagnosis. TB cases verified by the TB programs are reported to CDC using the software for expanded TB surveillance (SURVS-TB) and are included in CDC's TB surveillance statistics.

In contrast, in the 1993 AIDS surveillance definition, pulmonary TB includes definitive and presumptive diagnoses. Specifically, HIV/AIDS patients with a definitive diagnosis of pulmonary TB are patients who meet the criteria for the first component of the TB case definition (isolation of *M. tuberculosis* from a clinical specimen). HIV/AIDS patients with presumptive diagnoses of TB are patients who meet the criteria for the second (specimens positive for AFB, no culture) and third (clinical criteria) components of the TB case definition, as well as patients with TB cases verified by the TB program based on provider diagnosis.

Table 1 shows a comparison of the criteria for pulmonary TB in the TB surveillance case definition and the 1993 AIDS surveillance case definition.

All patients reported to the HIV/AIDS surveillance program with definitive or presumptive TB should be evaluated by the TB program. This is especially important for HIV-infected patients in whom the diagnosis of TB is based on a report of AFB in a clinical specimen, the clinical case definition, or provider diagnosis. AFB-positive specimens may contain mycobacteria other than *M. tuberculosis*, and these cases could be misclassified as TB if final culture

Table 1
Case Definition for Pulmonary TB
TB Surveillance vs. AIDS Surveillance

Criteria for TB Surveillance	Criteria for AIDS Surveillance
1. Cases for which *M. tuberculosis* is isolated from clinical specimen	
2. Cases for which AFB are found in clinical specimen when a culture has not been or cannot be obtained	
3. Cases that meet all of the following: • A positive tuberculin skin test result • Other signs and symptoms compatible with TB • Treatment with two or more anti-TB drugs • Completed diagnostic evaluation	4. Physician diagnosis of TB when above criteria are not reported

reports are not reviewed. In some patients, clinical syndromes consistent with TB may later be diagnosed as other conditions. These cases could be misclassified as TB if the complete clinical course of the patient has not been evaluated and the case verified by the TB program.

Cases may be evaluated by the TB program before they are entered into the HIV/AIDS Reporting System (HARS). Alternatively, cases may be entered into HARS, and if later evaluation by the TB program shows that they are not verified cases of TB, the report of TB should be removed from the AIDS surveillance registry. If the HIV-infected person has no other AIDS-defining conditions, the case should be removed from the AIDS surveillance registry. States that conduct HIV reporting should maintain this record for their HIV surveillance activities.

TB cases that are verified by the TB program are assigned an RVCT number by the state or local TB program. The RVCT number is a unique identifier for each TB case and is used when reporting TB cases to CDC. An RVCT number is not required for entering a TB report into HARS. However, if the RVCT number is not entered, HARS will issue this warning: "RVCTNO is needed for AIDS cases diagnosed with either definitive or presumptive pulmonary or extrapulmonary TB. Please retrieve this record later to update any necessary fields." If the RVCT number is not available at initial data entry, the HARS record should be updated when the RVCT number becomes available. The RVCT number is important because it facilitates communication between the AIDS and TB surveillance programs, and it ensures that cases are accurately reported to both systems.

Several states have laws and regulations that prohibit HIV/AIDS programs from sharing the HIV/AIDS status of TB patients with the TB program and from reporting patients with TB and AIDS to the TB program. Some areas affected by these laws have developed innovative approaches to facilitate the reporting of HIV/AIDS patients with TB to the TB program. For example, in one area HIV/AIDS program staff are encouraging the health care providers in each site where they do active AIDS surveillance to report to the TB program HIV-infected patients suspected of having TB. In addition, staff of the HIV/AIDS program and the TB program are conducting TB and AIDS case registry matches yearly or twice yearly. When AIDS patients with TB are not known to the TB program, HIV/AIDS program staff are assisting the health care providers in reporting the case to the TB program.

TB may be more difficult to diagnose among persons with HIV infection because of atypical clinical and radiologic presentations and/or the simultaneous occurrence of other pulmonary infections (e.g., *Pneumocystis carinii* pneumonia). Among persons with HIV infection, the difficulty in making a diagnosis may be further compounded by an impaired response to tuberculin skin tests and the low sensitivity of sputum smears for detecting AFB. TB and AIDS surveillance programs must become mutual ancillary sources of surveillance, and they should conduct cross training for their staff. Good collaboration between the TB and HIV/AIDS surveillance programs will promote the collection of accurate and complete information about patients coinfected with HIV and *M. tuberculosis.* This information will be useful in ensuring the best provision of services to HIV-positive persons with TB infection or disease. It will also help TB programs conduct prompt contact investigations to identify persons with TB infection or active TB who would benefit from treatment or preventive therapy.

—Reported by Eugene McCray, MD
Division of TB Elimination
and Jeff Jones, MD
Division of HIV/AIDS

References

1. CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR*. 1992;41(No. RR-17):1-19.

2. CDC. Update: impact of the expanded AIDS surveillance case definition for adolescents and adults on case reporting - United States, 1993. *MMWR*. 1994;43:160-61,167-70.

3. CDC. Case definitions for public health surveillance. *MMWR*. 1990;39(No. RR-13):39-40.

UPDATE FROM THE LABORATORY

Laboratory Training from CDC and the National Laboratory Training Network

A major objective of the National Action Plan to Combat Multidrug-Resistant TB is to increase the awareness of multidrug-resistant TB in the laboratory community and to upgrade the mycobacteriology capacity of public health laboratories. This includes training for mycobacteriologists in managerial and testing practices aimed at making laboratory testing more rapid, sensitive, and reliable. CDC and the National Laboratory Training Network (NLTN) provide TB-related training, as well as training products, to laboratories throughout the United States. The NLTN, a cooperative training system sponsored by the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD) and CDC, operates from 7 area field offices.

NLTN Training

In the last 2 years, the NLTN has given 29 TB laboratory training workshops to more than 1,500 participants in 26 states. In addition to these on-site workshops, the NLTN sponsored 3 TB teleconferences involving a total of 429 participants. In the teleconferences, a training program is broadcast simultaneously to multiple sites that are linked via telephone. For example, in January 1994 a BACTEC users group teleconference was simultaneously broadcast to 26 sites in 15 states; there were 146 participants. Usually, the programs are 1-2 hours long and they focus on a single TB-related topic, such as fastidious-growing mycobacteria or a users group discussion. A lecturer or a moderator leads the program. Training

materials, such as slides, lecture outlines, registration forms, and evaluation forms are sent to each site before the broadcast.

In 1994, the NLTN plans to offer seven TB-related, on-site workshops and eight teleconferences. For information on this and other NLTN training, call (800) 536-NLTN.

CDC-Based Training

Again this year, CDC will offer a formal, hands-on laboratory training course in advanced-level mycobacteriology to qualified laboratory personnel. The course content has been updated and modified to reflect current needs. The focus is on new radiometric and molecular testing methods that can produce test results more quickly. The course, Laboratory Methods in Medical Mycobacteriology, will be offered September 12-16, 1994, in Atlanta. A second course later in the month will be considered if the number of qualified applicants exceeds the limitations of class size. Ron Smithwick, Division of Bacterial and Mycotic Diseases, NCID, is the director of the course; Billie R. Bird, Division of Laboratory Systems, PHPPO, is the codirector. The teaching faculty is composed of experts from various centers and programs of CDC. Participants who successfully complete the course will be awarded 3.5 continuing education units. For information, call the course registrar, Quo Vadis Harris, at (404) 488-4202.

Training Products

Manuals. The manuals *Laboratory Manual for Acid-Fast Microscopy* (2nd ed. 1976); *Isolation and Identification of* Mycobacterium tuberculosis*: A Guide for the Level II Laboratory* (1981); and *Public Health Mycobacteriology: A Guide for the Level III Laboratory* (1985) are still available. For copies, call the NLTN at (800) 536-NLTN or National Technical Information Services at (703) 487-4650. These manuals do not contain information on rapid testing by radiometric or molecular methods.

Training packages. The NLTN has available two training packages that provide complete information for conducting specified laboratory training programs on TB. The contents include program objectives, a program schedule, lecture outlines, 2x2 Kodachrome slides, videotapes, and master copies of student handouts. The packages can be borrowed from the NLTN and copied.

Multidrug-Resistant Tuberculosis: The Laboratory DOES Make a Difference (1992) is a half-day program that focuses on methods of achieving a faster turnaround time for TB testing and reporting.

Isolation and Identification of *Mycobacterium tuberculosis* (1991) is a 2½-day hands-on workshop on the laboratory diagnosis of *M. tuberculosis* using conventional methods.

Audiovisuals. Each area resource office of the NLTN maintains a resource library of videotapes, sound-slide

programs, and slide sets. To borrow these training products, call the NLTN. Most can be copied while on loan.

Other NLTN training resources. The NLTN Training Calendar provides up-to-date listings of national and regional laboratory training activities. The Resource Directory lists laboratory training resources, such as self-study programs, videotapes, and slide sets. On request, the NLTN can provide a printout of the information by subject.

—Reported by Billie R. Bird
Division of Laboratory Systems
Public Health Practice Program Office

NEWS BRIEFS

- Parke-Davis is offering tuberculin skin test rulers. To order rulers, call Parke-Davis customer service at (800) 223-0432.

- The Texas Center for Infectious Diseases, a unit of the Texas Department of Health, will accept patients with TB and multidrug-resistant TB, including patients from outside of Texas. Treatment will be subject to the hospital's normal per diem cost of care. Preapproval must be obtained from Robert L. Treasure, MD, deputy director for professional services, at (210) 534-8857. The center also offers free telephone consultation on TB; the number is (800) TEX-LONG.

STUMP THE EXPERTS

Q: A physician prescribes a patient an initial regimen of isoniazid, rifampin, and pyrazinamide with the intention of discontinuing the pyrazinamide after 2 months. After 8 weeks, drug susceptibility tests reveal 100% resistance to isoniazid and rifampin. The physician discontinues the isoniazid, rifampin, and pyrazinamide and adds ethambutol, ofloxacin, and streptomycin.

We have been told that isoniazid

and rifampin are the only antituberculosis drugs that are bactericidal; all others are bacteriostatic. If this is true, then the new regimen would appear to be effective only in

stopping the further progression of disease, not in killing existing bacilli. How would this patient get cured?

A: Drugs are classified as bactericidal (able to kill bacteria) or bacteriostatic (able to inhibit the growth of bacteria) according to the results of in vitro tests. These tests do not include factors that occur in vivo, such as host defense mechanisms, the concentration of the drug in the cell, or the effect of other drugs in the regimen on the population of tubercle bacilli. Thus, the classification of antituberculosis drugs as bactericidal or bacteriostatic may not correlate with the contribution of these drugs to regimens used in clinical trials.

The effects of antituberculosis drugs and their roles in treatment regimens were studied by D.A. Mitchison in the 1970s and 1980s. Mitchison described two ways in which antituberculosis drugs affect tubercle bacilli in vivo: early bactericidal activity and sterilizing activity. Early bactericidal activity is the ability of a drug to decrease the number of actively multiplying tubercle bacilli in the sputum during the initial 14 days of therapy. In his studies, Mitchison found that isoniazid had the greatest early bactericidal activity, followed by rifampin and ethambutol. Streptomycin, pyrazinamide, and thiacetazone had the poorest effect.

Sterilizing activity is a term used to describe a drug's ability to decrease the number of semidormant bacilli ("persisters"). To assess sterilizing activity, Mitchison studied the rate of culture conversion for patients who had received 2 months of treatment with different drugs, as well as the relapse rate. He found that rifampin and pyrazinamide had the greatest sterilizing

activity, followed by isoniazid. Streptomycin, ethambutol, and thiacetazone had the least sterilizing activity. The striking sterilizing effect of pyrazinamide has been confirmed in clinical trials.

Mitchison concluded that early bactericidal activity affected the duration of infectiousness, whereas sterilizing activity influenced the length of treatment. Thus, the patient described in this question may receive adequate treatment with the prescribed regimen of ethambutol, ofloxacin, and streptomycin, but therapy would probably last longer than with a regimen containing isoniazid and rifampin.

Clearly, both early bactericidal activity and sterilizing activity are important to the design of treatment regimens. Another crucial factor is the ability of the drugs to prevent the emergence of drug resistance. Mitchison graded isoniazid and rifampin as having the greatest ability, ethambutol and streptomycin as having intermediate ability, and pyrazinamide and thiacetazone as having the least ability.

—Reported by Robin Huebner, PhD, MPH
and Pattie Simone, MD
Division of TB Elimination

BEHAVIORAL SCIENCE NOTES

The Use of Directly Observed Therapy by TB Programs

To ensure patient adherence to treatment and prevent the development of multidrug-resistant TB, CDC recommends that DOT be considered for all patients. In a recent survey of evaluation activities, conducted by Nilka Rios, an epidemiologist in the Prevention Effectiveness Studies Unit, Clinical Research Branch, 68 state, city, and territorial TB programs were asked about their use of DOT and the settings where DOT is delivered.

Preliminary data, based on 58 responses, show that DOT is used by the majority of programs surveyed, and that supervision is taking place in a variety of settings. In 48 programs (83%), DOT is delivered in the TB clinic; in 51 (88%), DOT is delivered in the patients' residences.

Programs also take advantage of many alternative settings. The most common alternative is best described as "hangouts": 23 programs (40%) deliver TB medications in bars, street locations, parks, or other informal locations. In 17 TB programs (29%), DOT is delivered in various health care settings, such as hospitals, emergency rooms, detoxification centers, and community health centers. Other alternative settings for DOT are worksites (11 programs), shelters (10 programs), and correctional facilities (10 programs). One program reported working with community-based organizations to deliver DOT, and another reported enlisting the help of responsible third parties to deliver DOT.

These data show that DOT is widely used and that programs are both innovative and realistic in attempting to administer medication while meeting the needs of patients. Although outside the scope of the survey, gathering information on the proportion of patients who receive DOT in various settings, as well as details on how DOT is carried out, would be valuable.

The results of this survey suggest possibilities for additional studies that would assist programs in deciding on the best method of delivering DOT. For example, is DOT more successful in one type of setting than another? Are patients more likely to show up in street settings that they choose themselves rather than in clinic settings? What factors could influence the success of DOT in worksites? Are alternative health care settings effective sites for DOT? Current studies under way at CDC will help determine the relative costs of various DOT strategies and describe the activities of outreach workers in different programs.

—Reported by Esther Sumartojo, PhD
Division of TB Elimination

INTERNATIONAL NOTES

A Review of the TB Screening Program in Vietnam

In January 1994 Nancy Binkin, assistant director for international activities, DTBE, accompanied staff of the Division of Quarantine, CDC, to South Vietnam to review the TB screening program for persons who wish to migrate to the United States. Because Vietnamese persons account for the third largest number of TB cases among immigrants to the United States, this trip provided an important opportunity to examine the efforts in Vietnam to screen and treat persons with TB before they arrive in the United States.

In Vietnam, which has a population of 57 million, the incidence of TB is approximately 150 per 100,000 persons. This is one of the highest incidences in the world. More than 1.2 million South Vietnamese have immigrated to the United States since 1975; last year, approximately 60,000 entered the United States.

The TB screening and treatment program has evolved considerably over the past several years. At present, the screening program is carried out by the International Organization for Migration (IOM), a group which also performs TB screening for the Australian and Canadian governments. Last year, they screened more than 70,000 applicants.

The medical staff consists of five full-time expatriate physicians and a laboratory technician. Screening is performed under the direct supervision of the IOM medical staff at two hospitals on a contractual basis. The facilities used for screening, including the x-ray department and the laboratory, are physically separate from the rest of the hospital. The Vietnamese staff of physicians, nurses, and laboratory and x-ray technicians are hospital employees, but they work only for the screening program.

All persons applying for immigration to the United States have a history and physical examination performed, and those 2 years of age and older are given a chest radiograph, which is read by the Vietnamese physicians conducting the screening. For all persons with chest radiographs potentially compatible with TB, early morning sputum specimens are collected on 3 consecutive days under direct supervision.

Sputum smears are examined right away by fluorescent microscopy. If organisms are seen, Ziehl-Neelsen counterstaining is performed, and a count of organisms is obtained. Any person found to have one or more positive smears is told to report for DOT. Persons with abnormal chest radiographs but negative smears who remain in Vietnam for more than 60 days are given another chest radiograph and sputum smear examination before departure. These persons are held in Vietnam for treatment if their sputum smears are positive. Cultures are not routinely performed, although efforts are under way to improve local culture capacity and the ability to perform susceptibility testing.

Directly observed therapy is conducted each morning at the two hospitals. Patients are asked whether they have ever received therapy for TB; those who deny having received therapy are given isoniazid, rifampin, pyrazinamide, and ethambutol 6 days a week for 2 months. Three consecutive, supervised early morning sputum specimens are then obtained. If the smear results are negative, pyrazinamide is discontinued and the patient receives isoniazid, rifampin, and ethambutol 6 days a week for 4 more months; sputum smears are examined again at the end of treatment. If the smear results are positive after the first 2 months of treatment, the four drugs are continued for 2 more months and repeat sputum smears are obtained. In addition, cultures are obtained and drug susceptibility testing is done if possible.

Patients whose smear results are still positive at the end of therapy, as well as

patients who have received previous therapy, are treated with seven drugs until 15 months after the smear results convert to negative. All patients are evaluated with a chest radiograph and a sputum smear examination shortly before leaving the country in order to ensure that they remain cured.

Potential immigrants and refugees, and in many cases their families, are not permitted to travel until the entire family has been medically cleared. As a result, the patients in this program are highly motivated to complete therapy, and few of them miss more than a couple days of therapy during their entire course.

However, such a system also means that there is a risk of fraud in the initial assessment of patients, and that persons who may have received previous treatment deny it because they do not want to jeopardize their application or because they know a longer treatment will be required. A number of safeguards have been put in place to decrease the likelihood of fraud. But despite numerous attempts by medical staff to question the patients, applicants continue to deny previous treatment. This has led to an unexpectedly high rate of treatment failure, despite the use of closely supervised therapy with an initial four-drug regimen.

Although the vast majority of the 500 persons treated each year are cured with the 6-month course of therapy, a number of patients have drug-resistant strains. No systematic culturing and drug susceptibility testing has yet been done on smear-positive persons at the time of diagnosis. In 1988-1990, the national TB program studied isolates from 425 supposedly new smear-positive patients in Ho Chi Minh City. Resistance rates were 35% for streptomycin, 19% for isoniazid, and 4% for rifampin. Overall, 43% of isolates were resistant to one or more drugs.

Drug resistance in persons applying for immigration may be due in part to medical examination and partial treatment in the private sector before the IOM physical. In addition, many of the persons applying for immigration receive antituberculosis drugs from sponsoring relatives who live overseas; because of the erratic therapy they receive, these applicants are at high risk for drug resistance. Another possible contributor to drug resistance in this group is treatment in the Vietnamese national program. Until recently, all patients in this program were treated with a standard regimen of 3 months of streptomycin, isoniazid, and pyrazinamide, followed by 6 months of streptomycin and isoniazid. Currently, the South Vietnamese program uses 2 months of streptomycin, isoniazid, pyrazinamide, and rifampin, followed by 6 months of isoniazid and ethambutol. The cure rate (the percentage of patients whose sputum converts from positive to negative by the end of treatment) has increased from approximately 68% with the old regimen to approximately 89% with the new regimen.

Because of logistical and staffing problems, isoniazid preventive therapy is not offered to all infected contacts of TB patients in the IOM screening program. Currently, preventive therapy is limited to contacts who are younger than 35 years old, have a skin test reaction of ≥10 mm, and live within 20 km of the treatment site. Preventive therapy is given daily for 6 months, although some patients leave for the United States before they complete therapy.

Overall, the dedication and professionalism of the IOM and local Vietnamese staff are impressive, and it appears that they are making every effort to ensure that those now coming to the United States are TB free. Furthermore, the cost per case treated is only $42, including smears, chest radiographs, and drugs. Paradoxically, the future of the program may be in jeopardy because of the normalized relationship between the United States and Vietnam. New diplomatic ties may necessitate a switch from IOM screening to less effective panel physician screening, as is conducted in the Philippines, India, and other countries, and DOT may not be possible.

—Reported by Nancy Binkin, MD, MPH
Division of TB Elimination

NEW PUBLICATIONS

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Cantwell MF, Shehab ZM, Costello AM, et al. Congenital tuberculosis. *N Engl J Med.* 1994;330:1051-1054.

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Colditz GA, Brewer TF, Berkey CS, et al. Efficacy of BCG vaccine in the prevention of tuberculosis. *JAMA.* 1994;271:698-702.

Jereb JA, Cauthen GM, Kelly GD, Geiter LJ. The epidemiology of tuberculosis. In: Friedman LN, ed. *Tuberculosis: Current Concepts and Treatment*. Boca Raton, Fla: CRC Press; 1994.

Simone PM. Multidrug-resistant tuberculosis. *Mediguide to Infectious Diseases.* 1994;14(1):1-8. For copies, write to Lawrence DellaCorte Publications, Inc.
919 Third Avenue
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attn: Stacey Ruhle

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Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. *N Engl J Med.* 1994;330:1179-1184.

PERSONNEL NOTES

Effective immediately, the Clinical Research Branch, DTBE, has been divided into two units: the Prevention Effectiveness Studies Unit, headed by Bess Miller, MD, MSc, and the Clinical and Diagnostic Studies Unit, of which Elsa Villarino, MD, is the acting chief. Dr. Villarino is also the deputy chief of the Clinical Research Branch.

Gustavo Aquino was chosen for the assistant public health advisor position in the New Jersey TB program. Gus began his career with CDC in 1990 in an assignment to the Miami Sexually Transmitted Diseases (STD)/HIV prevention program. He transferred to the Chicago STD/HIV prevention program in 1992. In January 1993 he joined the New York City TB program, where he has been a lead worker in the public health associate program. He transferred to Trenton on May 15.

Gail Burns was chosen for a new public health advisor position in New York City — the TB program manager in Brooklyn. Gail has been assigned to New York City since January 1993 as a first-line supervisor in the public health

associate program. Her first TB assignment was in Miami, starting in August 1991. She began her new duties on April 17.

Don Kopanoff, associate director for external relations, DTBE, retired from CDC on April 1, 1994. Don joined CDC in 1960 and served in various field assignments with the Division of Sexually Transmitted Diseases and the Division of TB Control (DTBC). He joined the headquarters staff of DTBC in 1967 as a member of the Training Unit, where he was instrumental in setting up several headquarters and field training courses, including TB Today. From 1974 to 1990, Don served as deputy chief, Clinical Research Branch. Don has received numerous awards, including an award for his assistance in forming the National Coalition to Eliminate TB.

Valecia Parker has accepted the position of secretary, office of the chief, Program Services Branch. Since July 1993, Valecia has been secretary to the chief, Behavioral Studies Section, Division of STD/HIV Prevention. She joined DTBE on April 18.

Pattie Simone, MD, was chosen for the position of deputy chief, Program Services Branch. Since July 1992, Pattie has been a medical officer in the Program Services Branch.

Vic Tomlinson has accepted the position of public health advisor in the Louisiana TB program. Since November 1992, Vic has been assigned to the Texas TB program; previously he had been assigned to the Missouri TB program. He transferred to New Orleans on May 15.

Rita Varga was selected for a new public health advisor position in New York City. Rita will be the training and career development manager in the public health associate program, a joint venture of DTBE and the New York City TB program. Rita came to work for CDC in 1986 and was assigned to the STD program in Indiana. She had subsequent assignments in Atlanta, Boston, and Chicago. Since June 1992, she has been the assistant training and career development manager in CDC's California STD/HIV prevention training center. She will transfer to New York City on June 26.

CALENDAR OF EVENTS

September 12-16, 1994
Laboratory Methods in Medical Mycobacteriology
Atlanta, Georgia
Quo Vadis Harris
National Center for Infectious Diseases, CDC
(404) 488-4202

October 4-7, 1994
34th Interscience Conference on Antimicrobial Agents and Chemotherapy
Orlando, Florida
American Society for Microbiology
(202) 942-9356

October 12-16, 1994
Frontiers in Mycobacteriology
Multidrug-Resistant Tuberculosis Where Do We Stand; Where Are We Headed?
Vail, Colorado
Dr. James Cook
National Jewish Center for Immunology and Respiratory Medicine
(303) 398-1359